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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,337	02/23/2004	Douglas J. Dellinger	10031505-1	8785

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AGILENT TECHNOLOGIES, INC.
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EXAMINER	
LUNDGREN, JEFFREY S	
ART UNIT	PAPER NUMBER
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/785,337	Applicant(s) DELLINGER ET AL.	
	Examiner Jeff Lundgren	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 4-6, 18 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 7-17, 19-21 and 23-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION***Election/Restrictions***

Applicant's election with traverse of the elected species in the reply filed on November 20, 2006, is acknowledged. The traversal is on the grounds that it would not be a burden to search all of the species. This is not found persuasive because each species represents a patently distinct species, where art related to anyone species would not necessarily anticipate another species. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-25 are pending; claims 4-6, 18 and 22 are withdrawn as being directed to a non-elected invention; claims 1-3, 7-17, 19-21 and 23-25 are the subject of the Office Action below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 7-17, 19-21 and 23-25, are rejected under 35 U.S.C. 102(b) as being anticipated by Guerlavais *et al.*, *Analytical and Bioanalytical Chemistry*, 374:57-63 (2002).

Claim 1 is directed to a method of analyzing a polynucleotide using matrix assisted laser desorption/ionization mass spectrometry, the method comprising a) obtaining the polynucleotide bound to a substrate via a linker moiety, the linker moiety comprising a triaryl methyl linker group wherein the polynucleotide is bound to a substrate via the triaryl methyl linker group; b) contacting the polynucleotide bound to the substrate with a matrix material; and c) analyzing the polynucleotide by matrix assisted laser desorption/ionization mass spectrometry.

Guerlavais teaches the use of MALDI-TOF mass spectrometry to characterize solid-supported oligonucleotides containing natural and non-natural and non-nucleoside moieties and a variety of internucleosidic linkages including phosphate and phosphite triesters and H-phosphonate diesters. This technique was used to follow the reactions involved in oligonucleotide synthesis; this enabled direct control of the elongation and optimization of the coupling process. Guerlavais teaches that his method is general and can be used to characterize

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still anchored ON bearing non-nucleosidic residues and a variety of internucleosidic linkages, including PIII H-phosphonate diester and phosphite triester linkages. MALDI can, moreover, be used to monitor oligonucleotide elongation step-by-step, thus enabling more rapid optimization of reaction conditions. Certain of the disclosed chemistries, namely, 5-O-Dimethoxytrityl-1,2-dideoxyribose-3-[(2-cyanoethyl)-(N,N-diisopropyl)]-phosphoramidite (page 58), meet the requirements of claims 1, 10-17, 19 and 20. See also Figure 2 on page 59.

As in claim 2 and 3, the oligonucleotide can be synthesized on the substrate.

Claims 1-3, 7-17, 19-21 and 23-25, are rejected under 35 U.S.C. § 102(b) as being anticipated by Koster et al., U.S. Patent No. 6,074,823, issued on June 1, 2000.

Claim 1 is directed to a method of analyzing a polynucleotide using matrix assisted laser desorption/ionization mass spectrometry, the method comprising a) obtaining the polynucleotide bound to a substrate via a linker moiety, the linker moiety comprising a triaryl methyl linker group wherein the polynucleotide is bound to a substrate via the triaryl methyl linker group; b) contacting the polynucleotide bound to the substrate with a matrix material; and c) analyzing the polynucleotide by matrix assisted laser desorption/ionization mass spectrometry.

Koster teaches a fast and highly accurate mass spectrometer based processes for directly sequencing a target nucleic acid (or fragments generated from the target nucleic acid), which by means of protection, specificity of enzymatic activity, or immobilization, are unilaterally degraded in a stepwise manner via exonuclease digestion and the nucleotides, derivatives or truncated sequences detected by mass spectrometry using MALDI-TOF. In Fig. 23, Koster teaches that nucleic acid immobilization is carried out using covalent bifunctional trityl linkers, and hydrophobic trityl linkers in Fig. 24. Koster states:

“In general, when it is the released nucleotide (or ribonucleotide) which is mass-modified, the modification should take as few steps as possible and be relatively efficient. For example, reactions used in adding base protecting groups for oligonucleotide synthesis can also be used to modify the released nucleotide just prior to mass spectrometric analysis. For instance, the amino function of adenine, guanine or cytosine can be modified by acylation. The amino acyl function can be, by way of illustration, an acetyl, benzoyl, isobutyryl or anisoyl group. Benzoylchloride, in the presence of pyridine, can acylate the adenine amino group, as well as the deoxyribose (or ribose) hydroxyl groups. As

the glycosidic linkage is more susceptible to hydrolysis, the sugar moiety can be selectively deacylated if the acyl reaction was not efficient at those sites (i.e. heterogeneity in molecular weight arising from incomplete acylation of the sugar). The sugar moiety itself can be the target of the mass-modifying chemistry. For example, the sugar moieties can be acylated, tritylated, monomethoxytritylated, etc. Other chemistries for mass-modifying the released nucleotides (or ribonucleotides) will be apparent to those skilled in the art.

In another embodiment, the linear, single-stranded DNA fragment can be anchored to a solid support. This can be achieved, for example, by covalent attachment to a functional group on the solid support, such as through a specific oligonucleotide sequence which involves a spacer of sufficient length for the ligase to react and which is covalently attached via its 5' end to the support (FIG. 1). A splint oligonucleotide with a sequence complementary in part to the solid support-bound oligonucleotide and to the 5' end of the linearized single stranded vector DNA allows covalent attachment of the DNA to be sequenced to the solid support. After annealing, ligation (i.e. with T4 DNA ligase) covalently links the solid support-bound oligonucleotide and the DNA to be sequenced. The splint oligonucleotide can be subsequently removed by a temperature jump and/or NaOH treatment, or washed off the support using other standard procedures. The solid support with the linear DNA is transferred to the reactor (FIG. 9) and contacted with an exonuclease in solution. As illustrated, where the 3' end of the unknown DNA fragment is exposed (i.e. unprotected), a 3' exonuclease is employed. The released nucleotides, or modified nucleotides, if intermediately contacted with a modifying agent such as alkaline phosphatase, are identified by mass spectrometry as described above. Other linking groups are described herein, and still others will be apparent to those skilled in the art based on the embodiments described herein. For example, the immobilization can occur through a covalent bond, such as a disulfide linkage, leuvinyl linkage, a peptide/oligo peptide bond, a pyrophosphate, a tritylether or tritylamino linkage, which can be cleaved in accordance with standard procedures (see e.g. Example 14 and FIG. 23). Immobilization can also be obtained by non-covalent bonds such as between biotin and streptavidin or hydrophobic interactions (see e.g. Example 15 and FIG. 24)."

Koster, col. 9, line 49 through col. 10, line 37.

Accordingly, claims 1-3, 7-17, 19-21 and 23-25 are anticipated.

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Conclusions

No claim is allowable.

If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipso verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Schultz, can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL



MARK L. SHIBUYA
PRIMARY EXAMINER